

REMARKS

Entry of this amendment, and reconsideration of this application, as amended, are respectfully requested.

Claims 29, 30, 42, and 43 have been amended to incorporate several signature mid-IR spectral band ranges as diagnostic markers for atherosclerotic disease. Support for these amendments can be found, for example, at page 5, paragraph [014], pages 16-19, Table 1 of the specification. Claim 34 has been amended to incorporate the features of the previous claim 35. No new matter has been introduced.

Claims 29-30, 32, 34-39, 42-47 and 50 were rejected under 35 U.S.C. §103(a) over U.S. Patent No. 6,697,665, alone, or over a combination of Rava and U.S. Patent No. 5,197,470 (Hefler). Claim 40 was rejected under 35 U.S.C. §103(a) over Rava in view of Helfer, as applied to claim 34, further in view of U.S. Patent No. 5,293,872 (Alfano). Claim 41 was rejected under 35 U.S.C. §103(a) over Rava in view of Helfer, as applied to claim 34, further in view of U.S. Patent No. 4,817,013 (Corenman). Claims 33 and 48-49 were rejected under 35 U.S.C. §103(a) over Rava in view of Helfer, as applied to claim 34, and further in view of U.S. Patent No. 6,129,667 (Dumoulin). Applicants respectfully traverse each of these rejections.

The presently claimed invention discloses methods and apparatus for *in vivo* detecting and characterizing conditions in abnormal tissues that present in vascular diseases, in particular, atherosclerosis, by using reflection-based mid-infrared (IR) spectroscopy. Specifically, the presently claimed invention teaches the use of signature mid-IR spectral bands as diagnostic markers for atherosclerotic disease.

Rava is cited by the Examiner as disclosing a spectroscopic method to obtain molecular vibration information with attenuated total reflectance (ATR) of infrared light. Applicants submit that the principles of ATR spectroscopy are completely different from those employed in the presently claimed invention; thus, Applicants submit that Rava is misapplied.

The reflectance spectra generated using ATR spectroscopy in Rava measures signals from the surface, with a penetration depth of less than 2 micrometers, see, e.g., col. 2, lines 58-59 of Rava ('[b]eing a surface technique...'), see also http://en.wikipedia.org/wiki/Attenuated_total_reflectance ("The penetration depth into the sample is typically between 0.5 and 2 micrometres..."). In contrast, the presently claimed

invention utilizes the reflectance and diffusive reflectance from inside the tissue or naturally formed reflectors inside the tissue caused by a disease, see, e.g., page 10, paragraph [039], lines 1-4 which states, “Unlike normal tissues that usually attenuate a large fraction, or even all of incoming MIR light, many constituents inside disease tissues including but not limited to atherosclerotic tissues are effective MIR reflectors that can transform the tissue into a highly reflective matrix.”

In addition, the ATR method described in Rava involves the subtraction of the strong water absorption from FT-IR ATR spectra. This step is essential for the ATR technology because in the mid-IR region, strong water absorption dominates the spectra of highly hydrated samples, thus obscuring the absorption from other tissue components, see, e.g., col. 2, lines 61-66 of Rava. Unlike Rava, the presently claimed invention is based on the principal that the presence of highly reflective crystalline and other fine-structure components in disease tissues together with the fact that non-native materials often contain very little water and transform the diseased tissue, such as atherosclerotic tissues, into effective MIR reflectors. Accordingly, the sensitive MIR reflectance and reflectance generated absorption spectroscopy may be used to diagnose a pathophysiological condition *in vivo*, see, e.g., paragraph [0041] of the specification, and the subtraction of water absorption is not essential in the presently claimed invention.

Since the ATR spectroscopy methods described in Rava measures signals from the surface while the signals from the pathophysiological conditions are from beneath the surface, the ATR technique employs an entirely different working principle from that of the presently claimed invention. Due to these substantial differences between Rava and the presently claimed invention, Applicants submit that a person of ordinary skill in the art would not have looked to Rava when contemplating the present invention in the first place.

Rava also discloses the use of infrared Raman spectroscopy. The differences between Raman spectroscopy and the tissue reflection-based mid-infrared (IR) spectroscopy of the presently claimed invention have been addressed extensively in the previous responses. In short, Raman bands refer to Raman shift, which, unlike the present invention, does not refer to reflectance or absorption at a specific wavenumber at all. Applicants note that in the outstanding office action, Rava is not cited by the Examiner for allegedly teaching infrared Raman spectroscopy. Therefore, Applicants assume that the Examiner has been convinced by Applicants’ prior argument that Raman spectroscopy differs from the reflection-based IR

spectroscopy employed in the present invention, *i.e.*, Rava cannot be considered to teach or suggest the use of the claimed signature mid-IR spectral bands to diagnose atherosclerosis.

Furthermore, with respect to claim 34, Rava fails to teach or suggest the reference wavenumber range stored in a computer means as set forth in claim 34. Such deficiency is not overcome by Helfer.

Since the two technologies, the ATR spectroscopy and Raman spectroscopy, employed by Rava are entirely different from the technology employed by the presently claimed invention, a skilled artisan would have no reason or motivation to consider Rava to arrive at the presently claimed invention. The deficiencies of Rava are not overcome by Helfer. Thus, all the obviousness rejections based on Rava and Helfer, *i.e.*, rejections over claims 29-30, 32, 34-39, 42-47 and 50, should be withdrawn based on the reasons set forth above.

Nonetheless, solely in order to advance prosecution and not in agreement as to correctness of the rejections of the claims, Applicants have amended the claims. Several signature spectral bands as diagnostic markers for atherosclerotic disease have been included in amended claims 29, 30, 34, 42 and 43. These signature spectral bands are not taught or suggested by Rava (see col. 10, TABLE I, col. 8 lines 10-17 of Rava) and the cited secondary references.

With respect to other §103(a) rejections of dependent claims 33, 40, 41, and 48-49, Applicants believe that the amendments to the independent claims moot the rejections of these claims. Furthermore, the deficiencies of the primary combination of Rava and Helfer are not overcome by other cited secondary references.

Therefore, Applicants submit that the claims are not obvious over Rava and the cited references and respectfully request that all §103(a) rejections be withdrawn.

In view of the foregoing, allowance is respectfully requested.

The Commissioner is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 50-0624, under Order No. NY-LBNL-238-US.

Respectfully submitted

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